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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/534,995	03/27/2000	Satoru Nishimura	0213-1431-0	4205

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EXAMINER
EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/534,995	NISHIMURA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,8-17 and 23-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-6,8-11, 13-15,17,23-27, 29-31, 33-35, 37-38 and 40-44* is/are allowed.

6)☒ Claim(s) *12,16,28,32,36 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-27-03 has been entered.

Response to Arguments

2. Applicant's arguments see Paper No. 25, filed 5-27-03, with respect to the rejection of claims 3-6, 9-12, 14-17, and 23-44 under 35 USC § 112, 1st paragraph, and the objection to claims 13-15, have been fully considered and are persuasive. The rejection of claims 3-6, 9-12, 14-17, and 23-44, and the objection of claims 13-15 have been withdrawn. However, the objection to claims 16-17 remains, and upon further consideration, a new ground(s) of rejection is made over claims 12, 16, 28, 32, 36 and 39 under 35 USC § 112, 1st paragraph.

Claim Objections

3. Claims 16-17 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot form the basis for another multiple dependent claim, either directly or indirectly. See MPEP § 608.01(n). Specifically, claim 10 (depends from claims 8 or 9), a multiple dependent claim, indirectly (i.e. through claim 12) serves as the basis for multiple dependent claims 16-17.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 12, 16, 28, 32, 36 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a tobacco plant expressing recombinant choline monooxygenase (CMO), that is resistant to high salt concentrations, which is correlated with dry or drought conditions, does not reasonably provide enablement for making every transgenic plants, other than tobacco, expressing recombinant CMO, wherein the transgenic plant is resistant to environmental stress conditions other than high salinity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification as filed provides only guidance for making transgenic tobacco plants which transgenically express recombinant choline monooxygenase from *Chenopodium album,* wherein said transgenic plant is capable of growing in high salt medium. The specification as filed, does not provide sufficient guidance and/or instruction that would allow the skilled artisan generate transgenic plants according to the present invention, wherein said transgenic plants are resistant to other forms of environmental stress, other than those associated with high salinity or drought conditions. For example, wherein said environment stress is associated with high light intensity, ultraviolet B radiation, heavy metal contamination in the soil, such as associated with lead, zinc, or nickel, flooding, wounding, infection with viruses, bacteria, or fungi, the

reactive oxygen species produced by these conditions, or herbicides (see Deak et al. Fromm et al., and Barocsi et al.). It is not clear from the specification as filed, or the prior art, that the expression of choline monooxygenase isolated from *Chenopodium album,* according to the present invention, in any plant, would be sufficient to render that plant resistant to any form of environmental stress, other than those associated with high salt concentrations. Neither the specification as filed, nor the prior art searched, provides any specific guidelines in this regard. The deficiencies in the specification would require undue experimentation since these steps must be achieved without instructions from the specification before one is enabled to practice the claimed invention.

In the instant case the amount of experimentation required to practice the full scope of the claimed invention would be undue based upon the following considerations. The factors to be considered in the determination of an enabling disclosure include, for example: the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. See MPEP § 2164.01(a).

Since there is no direct nexus between choline monooxygenase transgenic expression in plants and resistance to environmental stress factors that are not associated with high salt concentrations, the skilled artisan would have to resort to trial and error experimentation in order to identify unknown conditions wherein transgenic expression of choline monooxygenase expression in any plant would be suitable to produce resistance to all forms of environmental stress.

Moreover, there are multiple unpredictable factors associated with transgenic gene expression and the production of a particular phenotype. For example, contrary to

Applicant's results in the specification as filed, Nuccio et al. (1998; see page 490, Figure 5c) teach that expression of spinach choline monooxygenase in tobacco alone, did not produce high levels of glycine betaine in both stressed and salinized conditions, as observed in Applicant's results, see Figure 2. It was only when the CMO+ transgenic plants were supplied with 5mM choline or phosphocholine, that the transgenic plants accumulated both choline and betaine as observed by Applicants. Additionally, Nuccio et al. teach that it was impossible to predict whether transgenic CMA expression would produce a catalytically active enzyme since CMO activity requires correct assembly of the Rieske-type [2Fe-2S] center, and it was not clear that tobacco had all of the necessary components to assemble the active enzyme (see page 492, Discussion). This observation suggests that if a plant does not have all the necessary components, although a transgene may be present in the plant, it may not be able to produce active fully assembled CMO enzymes, and therefore would not produce the expected phenotype associated with said enzyme. This one example demonstrates the variable results associated with transgenic plants and the production of a particular phenotype.

Moreover, Flavell et al. teach that transgenes may produce unexpected phenotype alterations and instabilities, and in other cases transgene interactions may cause transcription silencing (see page 5). Additionally, Pawlowski et al. describe the irregular patterns of transgene silencing in transgenic plants. Pawlowski et al. state that "[t]ransgene expression remains largely unpredictable in most transformation experiments," and that "[S]everal factors related to integration and structure of transgene DNA, such as the number of transgene copies, position in the genome, and methylation, may greatly influence expression of transgenes. Transgene silencing, usually defined as

inactivation of transgene expression despite the present of an unchanged, but possible methylated, transgene sequence in the plant genome, was initially described in model plants such as tobacco and *Arabidopsis* transformed by *Agrobacterium tumafaciens.* More recently, transgene silencing has been observed in transgenic plants produced by particle bombardment.." (see page 597, Introduction).

Therefore, the amount of experimentation required to practice the full scope of the claimed invention would be undue in light of the high level of unpredictability associated with transgenic expression of proteins in plants, as taught by Nuccio et al., Flavell et al., and Pawlowski et al., the limited guidance provided in the specification as filed, and the broad scope of the claimed invention, namely wherein transgenic expression of CMO in plants would produce plants resistant to every form of environmental stress factor.

Conclusion

6. Claims 2-6, 8-11, 13-15, 17, 23-27, 29-31, 33-35, 37-38 and 40-44, are free of the prior art searched.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Fri, 8:30AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
August 6, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635